Whooping cough immunization in France and Britain: discussion paper[1]

E M Ross MD FRCP
L Edouard MSC MRCOG
Department of Community Medicine, The Middlesex Hospital Medical School
Central Middlesex Hospital, London NW10 7NS

Since the mid-1970s, the attitude in Britain of both the medical profession and parents towards whooping cough immunization has been in sharp contrast to that in France. As both countries have a similar-size population with many common characteristics and are separated only by a few miles of sea, we visited France to discover why these differences in practice and experience have occurred.

In Britain, vaccine trials were conducted in the late 1940s by the Medical Research Council, and an effective vaccine was introduced in 1951. The vaccine was soon widely administered although it did not become part of the nationally advised immunization policy until 1956. A decade later the vaccine was officially recommended by the French authorities, although pertussis vaccine had been in use in France since the late 1940s (Debre & Zourbas 1951).

The only vaccination which has ever been compulsory in Britain was smallpox; the law was not enforced for many years and was rescinded in 1948. In contrast, France has laws enforcing compulsory vaccination against diphtheria, tetanus, polio and tuberculosis (and regulations requiring smallpox vaccination at ages 11 and 21 remain statutory). There are prescribed penalties for those who fail to have their children immunized; however, these are rarely invoked and reliance is placed on health education. Vaccination against whooping cough, measles and rubella is recommended by the French State but is not compulsory. In a very few administrative areas, local health authorities have refused to administer whooping cough vaccine, but parents are able to have their children vaccinated by private medical practitioners.

In France, whooping cough vaccine is normally incorporated with diphtheria and tetanus toxoids as a triple vaccine, although it is sometimes administered either singly or as a quadruple vaccine in combination with killed polio. Starting at three months, the French whooping cough vaccination programme consists of three doses injected subcutaneously in the infraspinal fossa at monthly intervals, with a booster dose being advised about a year after completion of the primary course. A further booster dose is given at five years when there is a baby in the home. Only three injections at six-week intervals and starting at three months are advised in Britain: they are normally given by deep subcutaneous or intramuscular injection, usually into the deltoid or lateral thigh.

Up-to-date advice on all immunizations is clearly set out in an annual brochure of the Comité Français d'Education pour la Santé which gives details on the natural history of infectious diseases, nature of the vaccines as well as their potential complications and contraindications (Lambert 1981). We feel that there is a need for a similar publication in Britain and commend the booklet produced for local use in Sheffield (Hill & Bingham 1982).

Reported side effects of whooping cough vaccine in France (Rey 1980) include local inflammatory reactions thought possibly to be related to partial intradermic injection, fever up to 38.5°C, cough during the 48 hours after vaccination and cries or yelling during the six hours after injection, as well as more severe reactions such as collapse, convulsions and

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encephalopathy (Fillastre 1977, Fourquet 1978). Monnet (1981*a*) states that with all precautions taken, the risk of vaccine damage is less than that of a road traffic accident on the way from the child's home to the doctor's surgery.

Neurological complications of whooping cough vaccine were already suspected when the French vaccination programme was launched (Beaudoing *et al.* 1964). In the mid-1970s, a team at the Hospital for Sick Children, Great Ormond Street in London, reported 36 cases of neurological disorder which had followed within a month of pertussis immunization (Kulenkampff *et al.* 1974). These cases, which had been referred from a large number of centres over an eleven-year period, attracted a great deal of attention in the British and, to a lesser extent, the French medical press at the time.

A very similar study to that at Great Ormond Street was reported from the Hôpital Saint-Vincent-de-Paul in Paris by Aicardi & Chevrie (1975). They followed up, for a minimum of eight months, 20 children who had been admitted to their referral unit (from a very wide catchment area) who had either the first signs or a relapse of neurological disorder within seven days of pertussis immunization. All had convulsions, one died and 16 had continuing neurological sequelae when followed up for at least eight months. The 20 children included one with pre-existing hemiparesis, and another with a previous history of epilepsy. Four weighed less than 2500 g at birth. Although this paper has been widely quoted and was carefully studied by the French Ministry of Health, it was appreciated that it was not based on a defined population and made no claims that the vaccine caused the children's neurological problems. Although the authors made a plea that case-control studies should be undertaken, none have been reported from France. Addressing an international meeting in Paris, Stewart (1978) stressed that the incidence of neurological complication from pertussis vaccine was not known.

In Britain the press and television paid great attention to the paper by Kulenkampff *et al.* (1974), and demands for an enquiry into British pertussis vaccine policy were made in Parliament. The issue attracted enormous adverse publicity and led to a fall in vaccine uptake from a national 85% in the early 1970s to 30% by the end of the decade. As a result of this disquiet, a case-control study into serious neurological disease and infant immunization was commissioned by the Department of Health and Social Security. Although this study was govenment funded, it was carried out on an entirely independent basis at The Middlesex Hospital Medical School as the National Childhood Encephalopathy Study (Miller *et al.* 1981). This study sought every case of serious acute onset neurological disease of any type that could remotely be associated with immunization and that had required hospital admission in children aged 2–35 months living in England, Scotland and Wales in a three-year period starting in July 1976.

The attributable risk of neurological disease starting within a week of pertussis immunization in children who were previously neurologically normal was extremely low, being of the order of one in 100 000 immunizations, but the confidence limits were very wide. There were only 6 children with neurological disease still present twelve months later. The authors stressed that careful attention should be paid to the mathematical basis of their calculations and that the vaccine could be regarded as having a very low place in the causation of neurological disorders in British children.

Contraindications to pertussis vaccination

Contraindications, such as acute illness and immune deficiency states, are well accepted in both Britain and France. A past history of neurological illness such as encephalopathy or convulsion tends, in France, to be considered as a contraindication to whooping cough vaccination, although in milder cases practitioners are advised to administer an anticonvulsant and an antipyretic several hours before vaccination. This is strongly recommended in the case of institutionalized children, many of whom have neurological handicaps; it is felt that they are at particularly high risk of developing serious illness when they get whooping cough and immunization should be performed unless there is fever or

other signs of infection (Rey 1980, *Journal Officiel de Ministère de la Santé* 1966). In those with a history of allergy, some French practitioners would vaccinate under cover of a ten-day course of oral antihistaminics, starting on the day of vaccination. A history of allergy is not considered to be a contraindication in the United Kingdom.

Uptake of vaccination

In France, as in Britain, there are no national records of individual doses of vaccine given. The uptake of infant vaccines in France in general seems to have been unsatisfactory up to 1975. Since then an increased uptake has been attributed to better information and organization of child health surveillance. In 1979, 93.1% of children were recorded as having completed courses of diphtheria, tetanus and polio vaccines by the ninth month and 98.4% by the second birthday. It is estimated but cannot be confirmed that only 2% of the latter had not received pertussis vaccine.

Incidence of pertussis

French practitioners are under statutory obligation to notify cases of pertussis and to record the diagnosis on death certificates, but no fee is payable. From over 2000 notifications and 56 deaths in France in 1965, there has been a dramatic fall to current levels (*see* Table 1). Most of these deaths are in the first year of life. Although notification data are clearly unreliable and make it impossible to calculate the actual incidence of disease, secular trends provide a good indication of the occurrence of an epidemic. The sustained fall in the notification of pertussis in France since 1970 is in sharp contrast to the recent return of large epidemics in the UK. Despite the low French notifications, however, the number of deaths attributed to whooping cough is similar in the two countries (Table 1), giving an apparent case-fatality rate of 1 in 14 France as opposed to 1 in 3500 in England and Wales. Given that the two countries have broadly similar standards of living and quality of health care, it seems unlikely that the case-fatality rates would in reality be so vastly different. The implication then is that the great discrepancy in the notification rates is due to even grosser under-reporting of clinical disease in France than in England and Wales. (The level of interest in the disease in France may be lower than in Britain, but the derisory British notification fee of 25 pence can hardly be much of an incentive.) We have been unable to establish whether the French might have experienced an epidemic that has not been reflected in the official statistics, but the trends (Table 1) make this possibility unlikely.

Table 1. Notifications of and deaths from whooping cough

	Notifications of disease		Deaths registered with principal cause	
Year	France	England and Wales	France	England and Wales
1950	5051	157 752	593	394
1955	6738	79 133	388	87
1960	4309	58 030	156	37
1965	2673	12 945	56	21
1970	920	16 598	35	15
1975	372	8 913	7	12
1976	344	3 907	14	3
1977	184	17 475	8	7
1978	163	65 957	6	12
1979	170	30 816	11	7
1980	87	21 131	6	6
1981	66	19 395	4	5
1982	135	65 785	Not available	14

Compensation

In France, compensation for damage as a result of compulsory vaccination is governed by the law of 26 May 1975. It is presumed by jurisprudence that compensation will also apply to damage from combined vaccines that contain at least one compulsory component. So far, only three claims have been filed with respect to pertussis vaccine: two cases of acute anaphylactic collapse were awarded compensation, whereas the third was disallowed as it was considered to be due to a coincidental bacterial illness. These few claims are in striking contrast to the position in the United Kingdom where compensation has been awarded to more than 681 pertussis cases under the Vaccine Damage Payments Act of 1979 (Ferriman 1982). Payments are made in the United Kingdom to cases where the possibility of vaccine being responsible for the disability is greater than 50%. As incrimination of vaccine need not be beyond reasonable doubt, the number of compensated cases slightly exceeds the number predicted from epidemiological studies (Robinson 1981).

Comment

It is difficult to determine why the French and British experience with pertussis vaccine and the illness should differ so much. One of us (EMR) was given access to French documents relating to French vaccine policy and, having also had a lengthy discussion with appropriate French medical authorities, is convinced that the vaccine policy has been kept under frequent review since its introduction and that a watch is kept on experiences in other countries, particularly the United Kingdom and the United States of America.

There is unlikely to be any intrinsic difference in the composition of the vaccine in the two countries, as both manufacture it in accordance with World Health Organization standards, although there are differences between the adsorption agents used in some of the preparations made by the two French manufacturers, Pasteur and Merieux (Table 2). In the United Kingdom the vaccine is now made only by Wellcome and Glaxo. Griffith (1978) has stressed that there are some differences between the two vaccines, although there is no evidence that these result in identifiable findings in immunized children.

It is clear that there is far too little effective international cooperation over vaccine surveillance and development. It is absurd that there is no semblance of a European policy to protect children against this disease. As an illustration, Sweden discontinued pertussis vaccination on the grounds of ineffectiveness in 1979: yet Trollfors & Rabo (1981) have described pertussis disease in adults, and Taranger (1982) suggests that pertussis is becoming endemic among children.

Norway supports immunization against diphtheria, polio and tetanus. Denmark uses an unadsorbed monovalent pertussis vaccine in a regimen which begins at five weeks: uptake is around 88% whereas that of diphtheria, tetanus and polio is around 98%. In West Germany there has been much controversy about the use of the vaccine and we have been unable to

Table 2. Pertussis vaccines available in France. (Adapted from Monnet 1981b)

	Manufacturers			
	Pasteur		Merieux	
Vaccine combination	Adsorbed with	Injection volume (ml)	Adsorbed with	Injection volume (ml)
Pertussis only	Aluminium hydroxide	1	Not adsorbed	0.5
Diphtheria, tetanus and pertussis	Aluminium hydroxide	1	Aluminium hydroxide	0.5
Diphtheria, tetanus, pertussis and inactivated polio	Calcium phosphate	1	Aluminium hydroxide	0.5 for DTP (separate 0.5 ml for polio)

find a clear statement about national policy. We understand that its use is left to the judgment of family doctors who hold widely differing views. In East Germany pertussis immunization is compulsory. The United States, despite their litigious reputation, maintain very high pertussis vaccination rates and the disease is nearing extinction, many States using the canny device of requiring evidence of immunization before entry to school is permitted.

The present time, when computer-based vaccination schemes are being developed in many countries, particularly France (Martin-Bouyer *et al.* 1977) and Britain, presents new opportunities for cooperation. The need is heightened by the active development of a new generation of purer and potentially less toxic pertussis vaccines (Manclark 1981). Before they can be released, extensive and cautious clinical trials are going to be needed. It is not a moment too soon to begin to get the machinery ready. In the first place, the United Kingdom and France could begin formal collaboration. We were told that ours was the only known visit by a Briton to the Vaccine Department of the French Ministry of Health.

It seems that the main difference between France and Britain lies in the attitude of both public and profession towards both vaccine and disease. Whereas the British public and medical practitioners have been aroused by rare side effects of vaccine, the French medical practitioners seem comparatively indifferent towards incidence of disease and side effects of vaccine. We have failed to elucidate the reason for these paradoxical reactions which have unfortunately resulted in a decreased uptake of whooping cough vaccine and the ensuing public health problem in Britain.

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